

# **Allergic Diseases**

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# **Learning Objectives**

- **Identify symptoms, diagnosis and treatment courses for allergic and non-allergic rhinitis**
- **Recognize signs, symptoms, diagnosis, and treatment of food allergy**
- **Recognize signs, symptoms, and treatment for anaphylaxis**

# **Learning Objectives**

- **Identify mechanisms of drug allergy and its signs, symptoms, and treatment courses**
- **Determine signs, symptoms, and treatment courses for stinging insect allergy**
- **Determine diagnosis and treatment of urticaria and angioedema**
- **Understand hereditary angioedema**

# **Allergic Rhinitis**

- **Rhinitis- definition**
  - **Inflammation of the membranes lining the nose**
  - **Characterized by nasal congestion, rhinorrhea, sneezing, itching of the nose, and/ or post nasal drainage**
- **Allergic rhinitis- definition**
  - **Rhinitis that is caused by an IgE-mediated reaction to an aeroallergen**

# Allergic Rhinitis

- **Most common atopic disorder**
- **10-25% of population affected**
- **80% develop symptoms before age 20**
- **Impairs quality of life**
- **Affects school and work performance**
- **Cost greater than \$5 billion annually**



# Allergic Rhinitis

- **Symptoms**
  - **Rhinorrhea (clear)**
  - **Sneezing**
  - **Nasal congestion**
  - **Itching of nose, mouth, ears**
  - **Post nasal drip**
  - **Dry cough**
  - **Ocular symptoms**



# Allergic Rhinitis

- **Allergens (aeroallergens)**

- **Seasonal**

- **Tree, grass, weed pollens, molds**

- **Perennial**

- **Indoor allergens**

- **dust mite, cat, dog, cockroach, mold**

- **Occupational-latex, lab animals**



# **Allergic Rhinitis**

- **Seasonal allergic rhinitis - patterns**
  - **Spring – trees, grasses**
  - **Summer – grasses**
  - **Fall – weeds, molds**
  - **Winter–mold, Mountain Cedar in Texas**
  - **Varies somewhat by geographic location**



# **Allergic Rhinitis**

- **Pathophysiology**
- **1) Sensitization**
- **2) Early response**
- **3) Late response**

# **Allergic Rhinitis**

- **Sensitization**

- **Allergen exposure**
- **Allergen processed by APC's**
- **Antigen presented to T-cells**
- **T-cells make cytokines (IL-4 and IL-5)**
- **IL-4 causes B cells to make IgE antibody**
- **IL-5 recruits eosinophils**

# **Allergic Rhinitis**

- **Early Response**
  - **Repeat exposure to allergen**
  - **Antigen binds specific IgE on mast cells**
  - **Mast cells release preformed inflammatory mediators (e.g. histamine)**
  - **Symptoms occur within minutes**
  - **Causes vascular leaking (rhinorrhea)**
  - **Lacrimation, sneezing, itching**

# **Allergic Rhinitis**

- **Late response**
  - **4 -10 hours later more mediators released (newly synthesized)**
  - **Prostaglandins, leukotrienes**
  - **Eosinophils and basophils recruited to site of exposure**
  - **Cellular infiltration of tissues results**
  - **Symptoms of nasal congestion**

# **Allergic Rhinitis**

## **■ Diagnosis**

- History – timing, triggers, season, FH**
- Exam – eyes, nose, ears, pharynx**
  - Mucosa- pale, boggy, clear secretions**
  - Pharynx – post nasal drip**
- Identification of specific IgE**
  - Skin test – prick, intradermal**
  - RAST= radioallergosorbent test**

# **Allergic Rhinitis**

- **Differential diagnosis of rhinitis**
  - **Infection – viral, bacterial, other**
  - **Drug induced – aspirin, antihypertensive**
  - **Hormonal – pregnancy, puberty**

# **Allergic Rhinitis**

- **Other—Irritants, food, NARES (nonallergic rhinitic eosinophilic syndrome), polyps, emotional, atrophic, foreign body, CSF**
- **Non-allergic, non-infectious**

# **Allergic Rhinitis**

- **Treatment**
  - **Avoidance – environmental control**
  - **Antihistamines**
  - **Nasal steroid sprays**
  - **Anti-leukotrienes**
  - **Decongestants**
  - **Immunotherapy**



# **Allergic Rhinitis**

- **Antihistamines - Block H1 receptor**
  - **Nonsedating/second generation**
    - **Fexofenadine [generic] or Allegra®**
    - **Loratidine [generic] or Claritin®**
  - **Minimally sedating/second generation**
    - **Cetirizine [generic] or Zyrtec®**

# **Allergic Rhinitis**

- **Decrease rhinorrhea, pruritis, sneezing**
- **Not very effective for congestion**

# **Allergic Rhinitis**

- **Antihistamine – 1<sup>st</sup> generation**
  - **Sedating**
  - **Impaired reaction time, learning**
  - **Anticholinergic side effects: dry mouth, eyes, urinary retention; caution in elderly**

# Allergic Rhinitis

- **Diphenhydramine [generic] or Benadryl®**
- **Chlorpheniramine [generic] or Chlor-trimeton®**
- **Hydroxyzine [generic] or Atarax™**

# **Allergic Rhinitis**

- **Nasal steroid sprays**
  - **Antiinflammatory – shrink nasal mucosa**
  - **More effective than any monotherapy**
  - **Helpful in patients with nasal polyps**
  - **Slower onset; daily use required**

# **Allergic Rhinitis**

- **Effective on rhinorrhea AND congestion**
- **Side effects: epistaxis, headache, dry nasal mucosa**

# **Allergic Rhinitis**

- **Anti-leukotrienes**
  - **Also called leukotriene modifiers, leukotriene receptor antagonists**
  - **e. g., Montelukast [generic] or Singulair®, Zafirlukast [generic] or Accolate®**

# **Allergic Rhinitis**

- **Effective in allergic rhinitis and asthma**
- **Combination with antihistamine better than either agent alone**



# **Allergic Rhinitis**

- **Immunotherapy**
  - **Allergen specific therapy**
  - **Most effective for pollens**
  - **Only form of treatment that can alter the immune response**
  - **Potential long-term cure of disease**
  - **Time commitment of 3-5 years**
  - **Risk of anaphylaxis**

# **Allergic Rhinitis**

- **Allergic conjunctivitis (seasonal/perennial)**
  - **Often accompanies allergic rhinitis**
  - **Due to pollens, pet allergens, dust mite**
  - **Symptoms include ocular itching, redness, increased lacrimation, white stringy exudate,**
  - **Up to 30% of patients only have ocular symptoms**

# **Allergic Conjunctivitis**

- **Treatment**
  - **Ocular antihistamines**
    - **Olopatadine [generic] or Patanol®**
  - **Ocular mast cell stabilizers**
    - **Lodoxamine [generic] or Alomide®**
  - **Ocular antihistamine/decongestant**
    - **Naphazoline [generic] or Naphcon®, Vasocon®**

# **Other Allergic Eye Disorders**

- **Atopic keratoconjunctivitis**
  - **Chronic inflammation of the eye (lower lid conjunctiva)**
  - **Severe itching burning, tearing**
  - **Associated with atopic dermatitis (95%) and asthma (85%)**
  - **Can cause anterior cataracts**
  - **Tranta's-Horner's dots- discrete swelling with white dots around iris**

# **Other Allergic Eye Disorders**

- **Vernal keratoconjunctivitis**
  - **Chronic, severe conjunctivitis-**
    - **upper lid, cobblestone papillae**
  - **Frequent onset in Spring/Summer**
  - **Symptoms of intense pruritus, milky fibrinous exudate, photophobia**

# **Other Allergic Eye Disorders**

- **Tranta's Horner's dots**
- **Can cause blindness if involves cornea**

# **Allergic Conjunctivitis**

- **Giant Papillary Conjunctivitis**
- **Associated with contact lens use**
- **Symptoms of mild pruritus, abnormal thickening of conjunctiva, mucus stranding**
- **Giant papillae and micropapillae on the upper tarsal conjunctiva**
- **Reaction to foreign proteins on surface of contact lens**

# **Allergic Rhinitis**

- **Oral Allergy Syndrome**
  - **Occurs in 30-70% of patients with pollen allergy**
  - **Symptoms occur after oral mucosa contacts certain foods (fruits, celery)**
  - **Symptoms are itching of palate, throat, lips; may lead to angioedema in minority**
  - **Due to cross-reactivity between pollens and substances in certain foods**



# Allergic Rhinitis

- **Oral allergy syndrome - examples**
- **Ragweed – banana, melons, watermelon**
- **Birch pollen – apple, cherry, peach, celery, hazelnut, pear**
- **Treatment**
  - **Avoidance of offending food**



# **Non-allergic Rhinitis**

- **Similar symptoms as allergic rhinitis**
- **Not due to IgE or allergens**
- **Mechanism not well understood**
  - **Nasal hyperresponsiveness**
  - **Vascular dilation causes congestion**
  - **Often called “vasomotor rhinitis”**
- **Triggers - Strong odors, alcohol, spicy foods, emotions, hormones**

# **Non-allergic Rhinitis**

- **Treatment**
  - **Nasal steroid sprays**
  - **Decongestants (pseudoephedrine)**
  - **Nasal saline irrigation or sprays**
  - **Aselastine [generic] or Astelin® nasal spray for congestion – antihistamine but it helps**
  - **Ipratropium bromide or Atrovent® nasal spray for rhinorrhea**

# **Non-allergic Rhinitis**

- **Treatment – continued**
  - **Avoid decongestant nasal sprays  
Oxymetazoline or Phenylephrine  
[generics]**
  - **More than 3-5 days can lead to  
rebound congestion (“rhinitis  
medicamentosa”)**

# **Non-allergic Rhinitis**

- **New therapies**
  - **Intranasal capsaicin - painful**
  - **Tachykinin receptor antagonists**

# **Food Allergy**

- **Prevalence – often overestimated**
  - **25% of adults felt they had an adverse food rxn**
  - **28% of moms felt their child had food allergies**
- **Overall prevalence of food allergy**
  - **Children: 4-8%**
  - **Adults: 1-2%**

# **Food Allergy**

- **Prevalence**
  - **Higher in select population**
  - **Atopic dermatitis**
    - **Up to 35% have food allergy**

# Food Allergy

- **Most common food allergens**
- **Children**
  - **Cow's milk, wheat, soy, egg, and peanut**
  - **Account for 90% of reactions**
- **Adults**
  - **Peanuts, tree nuts, fish and shellfish, egg, fruits and vegetables**





# Food Allergy

- Incidence
- Cow's milk: 2.5%
  - >75% tolerant by 3rd birthday
- Egg allergy: 1.3%
  - >85% tolerant by 3rd birthday



# Food Allergy

- **Peanut allergy:**  
**0.5-0.7%**
  - **Clinical tolerance reached in only a minority of patients (10-20% with initial reaction of minor skin symptoms only)**



# **Food Allergy - Definitions**

- **Adverse food reaction - any aberrant reaction after ingestion of a food or food additive**
- **Toxic reactions – due to toxin (bacterial, other) present in a food**
- **Nontoxic reactions - depends on individual susceptibilities**
  - **Immune - allergy or hypersensitivity**
  - **Nonimmune - intolerances**

# **Food Allergy**

- **Immune reactions**
- **Gell and Coombs Classifications**
  - **Type I: IgE-mediated**
  - **Type II: antibody-dependent cytotoxicity**
  - **Type III: antigen-antibody complex**
  - **Type IV: cell-mediated**
- **True food allergy is Type I, IgE mediated**

# **Food Allergy**

- **Nonimmune**
  - **Due to pharmacological properties of the food (caffeine or tyramine)**
  - **Unique susceptibility of the host (lactase deficiency)**
  - **Idiosyncratic**
  - **Ex: Chinese restaurant syndrome**

# **Food Allergy**

- **IgE mediated reactions –clinical symptoms**
- **Cutaneous**
- **Diffuse pruritis**
- **Acute Urticaria +/- angioedema**

# Food Allergy

- **Exacerbations of atopic dermatitis**
  - **Implicated in 35% with moderate to severe atopic dermatitis**
  - **Common offenders – egg, peanut, milk, soy, wheat, fish**



# **Food Allergy**

- **IgE mediated reactions**
- **Gastrointestinal symptoms**
  - **Nausea, vomiting most common**
  - **Abdominal pain, cramping, flatulence**
  - **Diarrhea**
  - **Infantile colic**
  - **Allergic eosinophilic gastroenteritis**



# **Food Allergy**

- **IgE mediated reactions – continued**
- **Respiratory reactions**
  - **Rhinoconjunctivitis**
  - **Asthma**
- **Respiratory symptoms alone are rare**
- **Usually part of systemic anaphylaxis**

# **Food Allergy**

- **IgE mediated reactions-continued**
- **Generalized Anaphylaxis: Most common cause of anaphylaxis in ERs**
- **Skin: urticaria/angioedema**
- **Respiratory: rhinitis/bronchial hyperreactivity**

# **Food Allergy**

- **Cardiac:**  
**hypotension/arrhythmias/vascular collapse**
- **GI: nausea/vomiting/abdominal cramping/diarrhea**

# Food Allergy

- Food dependent, exercised-induced anaphylaxis
- Rare
- Occurs 2-4 hrs after ingestion of specific food
- Teens to late 30's
- Male : female = 1:2
- Common offenders: wheat, celery, shellfish, fish, fruits, milk



# **Food Allergy**

- **Diagnosis**
- **Careful history with emphasis on reaction**
- **Selective skin testing or RAST if suspect IgE-mediated**
- **Appropriate exclusion diet**
- **Blinded provocation**

# **Food Allergy**

- **History details**
- **Food suspected**
- **Quantity ingested**
- **Reproducibility/recurrence**
- **Time from ingestion to onset of symptoms**
- **Other factors (exercise)**
- **Length of time since last reaction**

# **Food Allergy**

- **Diagnostic testing**
- **Skin testing**
  - **NPV >95%**
  - **Good at excluding IgE-mediated food allergies if negative**
  - **PPV <50%; (i.e. 50% are false positives)**

# **Food Allergy**

- **RAST**
  - **Considered less sensitive than skin testing**
  - **Recommend Pharmacia CAP-RAST**
  - **Useful if skin tests contraindicated**
    - **Dermatographism**
    - **Severe dermatitis**
    - **Inability to stop antihistamines**
    - **High risk of anaphylaxis**



# **Food Allergy**

- **Food Challenge**
- **Double-blind, Placebo-Controlled Food Challenge is the gold standard test for diagnosing food allergy**
  - **Eliminate suspected foods 7-14 days prior to testing**
  - **Hold antihistamines**

# **Food Allergy**

- **Administer increasing amounts of food or placebo**
- **Disguise foods in: gelatin capsules, milk shakes, applesauce**
- **Observe patients for reactions and treat**
- **Negative challenge must be confirmed with open challenge under observation**

# Food Allergy

- **Treatment**
- **Strict elimination of offending agent**
- **Emergency care plan**
  - **Written anaphylaxis action plan**
  - **Injectible epinephrine**
  - **Medic Alert bracelet**
- **Annual f/u with Allergist**



# **Food Allergy**

- **Tips for avoidance of foods at school**
- **Education**
  - **Patient, parents, school nurse, teachers**
- **Safe snacks**
- **Minimize contamination**
- **Discourage trading food**

# **Food Allergy**

## **Allergic eosinophilic gastroenteritis**

- **Infiltration of esophageal, gastric, or intestinal walls with eosinophils**
- **Abdominal pain, early satiety, vomiting, FTT**
- **IgE-mediated reactions implicated, likely other mechanisms involved as well**
- **Diagnosis confirmed by biopsy**

# **Food Allergy**

- **Non-immune food reactions**
- **Toxic**
  - **Toxins from Salmonella, Shigella, and Campylobacter species**
  - **Scromboid fish poisoning - contamination with Klebsiella or proteus → decarboxylation of histadine to histamine**

# **Food Allergy**

- **Non-immune food reactions**
- **Non-toxic**
- **Pharmacologic reactions**
  - **Vasoactive amines (caffeine, tyramine, phenylethylamine, serotonin, theobromine)**
    - **Headache, palpitations, abdominal discomfort**

# **Food Allergy**

- **Idiosyncratic reactions**
  - **Bisulfites**
    - **Asthma by inhalation of sulfites from chewed foods**



# Food Allergy

- **Salad bars, sparkling wines or juices, beer, cheeses, dried fruits, pickles**



# Food Allergy

- **Dyes**
  - **Asthma and urticaria – mechanism unknown**



# **Food Allergy**

- **Idiosyncratic reactions - continued**
  - **MSG**
    - **Chinese restaurant syndrome – mechanism unknown**
  - **Lactose intolerance (lactase deficiency)**
    - **Fermenting lactose -> bowel gas, abdominal discomfort, diarrhea**

# Food Allergy

- Celiac disease – gluten sensitive enteropathy
- Malabsorption syndrome from wheat, barley, rye, oats
- Diagnosis
  - Labs - antigliadin Ab, antiendomysial Ab
  - Intestinal biopsy
- Treatment – avoidance of wheat, barley, rye, and oats



# Food Allergy

- **FOOD ALLERGY & ANAPHYLAXIS NETWORK**
- [www.foodallergy.org](http://www.foodallergy.org)

# **Anaphylaxis**

- **Richet and Portier (1902) coined term anaphylaxis**
  - **Against “phylaxis” - protection**
- **2 criteria**
  - **Increased sensitivity after previous exposure**
  - **Incubation period in which it develops**

# **Anaphylaxis**

- **Anaphylaxis is a life-threatening allergic reaction to a foreign antigen**
- **Mediated by IgE antibody located on membranes of mast cells and basophils**
- **Resulting in the release of preformed mediators which cause the systemic reaction**

# Anaphylaxis

- Mechanism
- IgE-mediated release of mast cell products
  - Hymenoptera, food, PCN, latex



PCN





# Anaphylaxis

- **Non-IgE-mediated = “anaphylactoid”**
  - **Complement mediated (Immune complex => anaphylatoxins)**
  - **Antibody mediated mismatched blood transfusions;  
IV gammaglobulin**



# **Anaphylaxis**

- **Mechanism – Non-IgE-mediated continued**
- **Nonimmunologic mast cell activators also called “pseudo-allergic reaction”**
  - **Opiates/narcotics, RCM, dextrans, neuromuscular blockers, Vancomycin [generic] (Red Man Syndrome)**

# **Anaphylaxis**

- **Mechanism – Non-IgE-mediated continued**
- **Nonimmunologic mast cell activators also called “pseudo-allergic reaction”**
  - **Opiates/narcotics, RCM, dextrans, neuromuscular blockers, Vancomycin [generic] (Red Man Syndrome)**

# Anaphylaxis

- **Examples:**
  - Food
  - Hymenoptera
  - Drugs
  - Latex
  - Exercise
  - Idiopathic
  - Immunotherapy



# **Anaphylaxis**

- **Incidence and prevalence data limited**
- **Most common causes are antibiotics (PCN) and radiocontrast agents**
  - **Penicillin (PCN) accounts for 75% of deaths in U.S. due to anaphylaxis**
  - **1 reaction per 5000 exposures**
  - **Account for the majority of deaths**
  - **< 10% of reactions are fatal**

# Anaphylaxis

- **Hymenoptera stings are next most common**
  - **25% of population may be at risk--tens of thousands of reactions**
  - **Less than 100 deaths per year**



# Anaphylaxis

- Risk of recurrent reaction with reexposure
  - PCN 10-20%
  - Radiocontrast media 20-40%
  - Insect stings 40-60%



# **Anaphylaxis**

- **Presentation**
- **Rapid onset (seconds-minutes)**
- **May be biphasic (i.e. late phase response)**
- **Cutaneous—**
  - **Flushing**
  - **Pruritis**
  - **Urticaria**
  - **Angioedema**



# **Anaphylaxis**

- **Respiratory**
  - **Upper--stridor, hoarseness, dysphonia from laryngeal edema**
    - ▶ **OBSTRUCTION** ▶ **DEATH**
  - **Lower--dyspnea, wheezing, chest tightness, coughing**
- **Cardiovascular**
  - **lightheadedness, tachycardia**
    - ▶ **shock**

# **Anaphylaxis**

- **GI--N/V/D, GI cramping, or dysphagia**
- **GU--uterine cramping**
- **Neurological--confusion, LOC, seizures**
- **HEENT--naso-ocular sx's**
- **Other--fear of impending doom and metallic taste**

# **Anaphylaxis**

- **Differential Diagnosis**
  - **Vasovagal reactions**
  - **Hereditary angioedema**
  - **Serum sickness**
  - **Carcinoid syndrome**
  - **Systemic mastocytosis**
  - **Pheochromocytoma**
- \*May measure tryptase levels in difficult cases**

# **Anaphylaxis**

- **Management: General principles**
- **Rapid recognition of anaphylaxis and assessment of severity**
- **Epinephrine (# 1 treatment; Do first!)**
- **Establish and maintain airway (safety net)**

# **Anaphylaxis**

- **Fluid resuscitation**
- **Secondary medication**
- **Identification of inciting agent**
- **Prevention and avoidance**

# **Anaphylaxis**

- **Epinephrine**
  - **Primary and most important treatment**
  - **Delay in epinephrine risk factor for death**
  - **Airway obstruction is the most common cause of death**

# Anaphylaxis

- **Dose**
  - **Adults 0.3 - 0.5 ml IM (1:1000)--  
repeat in 5-20 min if needed**
  - **Children 0.01mg/kg IM**

# Anaphylaxis

- **ESTABLISH AIRWAY** and supplemental  $O_2$
- **IV fluids**





# Anaphylaxis

- **Epinephrine**
- **When, how, and how much to give?**
- **IM provides faster absorption and higher blood levels than SQ**
- **Better to give early**
- **Less effective once in cardiovascular collapse**

# **Anaphylaxis**

- **Fatal and near-fatal anaphylactic reactions to food in children and adolescents**
- **13 children with anaphylaxis to food**
- **All with known food allergies**
- **6 died**
- **7 intubated**

**Sampson, NEJM 1992;327:380-4**

# **Anaphylaxis**

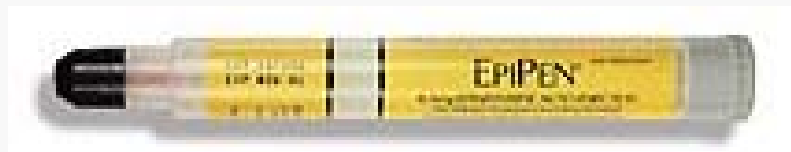
- **Sampson study continued:**
- **6 fatal**
  - **Symptoms 3-30 minutes**
  - **Only 2 had epinephrine in first hour**
    - **25 and 60 minutes**
- **7 non-fatal**
  - **Symptoms within 5 minutes**
  - **7/7 received epinephrine within 30 minutes**

# Anaphylaxis

- **Prescribing epinephrine:**
- **Epi-pen is easiest device to use**
- **Epi-pen = 0.3 cc of 1:1000 conc.**
- **Epi-pen Jr (up to 66 lbs) = 0.15 cc**
- **Instruct on indications**
- **Demonstrate how to use**
- **Patient to call 911 or go to ER after use**
- **Always prescribe 2!**

# Anaphylaxis

- **Epi-Pen Instructions**
  - **Form fist around auto-injector**
  - **Pull out the gray safety cap**
  - **Place the black tip near the outer thigh**
  - **Press firmly into lateral thigh**
  - **Hold in place for 10 seconds**
- **On side of Epi-pen with diagrams**



# **Anaphylaxis**

- **When to repeat epinephrine?**
- **Summary Statement AAAAI: Repeat every 10-15 minutes in adults and every 15 minutes in children**
- **UK Consensus Panel on emergency Guidelines and International consensus guidelines for emergency cardiovascular care: Epinephrine may judiciously be repeated as often as every 5 minutes**

# **Anaphylaxis**

- **Treatment – second line agents**
- **Antihistamines**
  - **H1 blocker**
  - **H2 blocker**
- **Corticosteroids (?? prevent late phase 6-8 hrs)**

# **Anaphylaxis**

- **Second line agents (cont')**
  - **B2 agonists (bronchoconstriction)**
  - **Miscellaneous**
    - **Severe hypotension  
(vasopressors and volume  
expanders)**



# Anaphylaxis

- **If on beta blocker, consider glucagon (1 mg bolus with continuous infusion of 1 – 5 mg/hour)**

# **Anaphylaxis**

- **Risk factors for poor response to therapy**
  - **Asthma**
  - **Beta blockers**
    - **Blocks the B1, B2 anti-anaphylactic actions of epinephrine**
    - **Unopposed alpha blockage may cause constriction of coronary arteries, elevation of blood pressure**
  - **Elderly patients w/cardiovascular disease**

# **Anaphylaxis**

- **Considerations**

- **How will the pt do if the same reaction occurs in 6-8 hours?**
- **How far does the patient live from the hospital?**
- **Does the patient live alone?**
- **Other major medical problems? Poor reserve?**

# **Anaphylaxis**

- **Epi-pen : DEY Pharmaceuticals,  
Napa, CA**
  - **(800) 755-5560**
  - **They will send trainer devices**
- **MedicAlert Bracelet, Necklace**
  - **(800) 432-5378**

# **Anaphylaxis**

- **Prevention:**
- **Avoidance of causative agents**
- **Avoid beta-blockers in high risk patients**
- **Preventative protocols**
  - **Pretreatment for IV dye loads in pt with dye allergy**
  - **Wash blood products in IgA deficient patients**

# Drug Allergy

- Adverse reactions to drugs are common
- “Allergy” or hypersensitivity to a drug is defined as “any immunologic response to a drug or its metabolites that results in an adverse reaction”
- Most allergic reactions require previous sensitization
  - Exception when drugs share antigenic determinants

# **Drug Allergy**

- **Immunologically-mediated reactions represent up to 10% of observed adverse drug reactions in inpatients**
- **Individual risk of allergic reaction to a drug is 1-3%**
- **Drug associated fatalities reported in 0.1% of medical inpatients**
- **Fatal drug reactions often have allergic features**

# **Drug Allergy**

- **Generally drug reactions are classified into 2 broad categories:**
  - **Type A: Common and predictable reactions that can occur in any patient**
  - **Type B: Uncommon and unpredictable reactions occurring in only susceptible patients**



# Drug Allergy

- **Type A Reactions**
- **Account for 80% of adverse drug reactions**
- **Typically dose-dependent**
- **Produced from pharmacologic action of drug**
- **These reactions are commonly called: *toxicity, side effects, teratogenic effects, drug-drug interactions***

# Drug Allergy

- Type B - the minority of drug reactions
- Not related to the drug's pharmacologic actions and not dose-dependent
- Labeled *intolerance, idiosyncratic reactions, allergic and “pseudoallergic” reactions*
- Idiosyncratic reactions may be difficult to distinguish from allergic reactions

# **Drug Allergy**

- **Type B reactions – examples**
- **Intolerance – tinnitus due to aspirin**
- **Idiosyncratic – Coumadin® induced skin-necrosis in pt with protein C def.**
- **Allergic – penicillin (IgE-mediated)**
- **Pseudoallergic – radiocontrast media (direct mast cell degranulation)**

# **Drug Allergy**

- **Allergic drug reactions - characteristics**
  - **High molecular weight drugs (insulin, antisera); low molecular wt drugs (PCN)**
  - **Proteins allergens**
  - **Inflammation already present (adjuvant which enhances immunologic response)**
  - **Prolonged or repeated therapies**
  - **Certain genetic HLA phenotypes or predisposed individuals (atopic)**

# Drug Allergy

- ***Allergic or hypersensitivity* drug reactions are immunologically-mediated and share the following characteristics:**
  - **Occur in small numbers of patients**
  - **Require previous sensitization**
  - **Develop rapidly after re-exposure**
  - **Produce clinical syndromes associated with immunologic reactions**

# **Drug Allergy**

- **Gell and Coombs Type I: IgE-mediated mast cell degranulation and newly formed mediators causing anaphylactic reactions usually within 30 min after drug administration (urticaria/angioedema, wheezing)**
  - **Diagnosis w/ history/PE/skin/testing/RAST**
  - **Treatment with avoidance vs. desensitization**

# Drug Allergy

- Type II: Cytotoxic reactions mediated by binding IgG, IgM to cell bound antigens, leading to activation of complement destroying cell to which antigen is bound
  - Examples: Coombs' positive hemolytic anemia, AIN, pneumonitis
  - Diagnosis by clinical syndrome, *in vitro* demonstration of antibody
  - Treat by removing offending agent/steroids

# Drug Allergy

- Type III: Immune-complex mediated by antigens binding to antibodies (IgG and IgM, subsequent tissue deposition and complement activation)
  - Serum sickness is a classic example (skin eruptions [urticarial/morbilliform], fever, arthralgias, LAD, GN, vasculitis)
    - Serum sickness usually 7-21 days after drug started



# Drug Allergy

- **Type III Treatment: Remove offending agent/steroids. Future administration of agent is relative contraindication**

# Drug Allergy

- Type IV: Delayed hypersensitivity mediated by T-cells, cell mediated immunity
- Examples: some forms of AIN, contact dermatitis, drug fever and drug-induced vasculitis
  - Diagnosis by clinical syndrome, patch test (for topical substances), *in vitro*
  - Treatment: Removal of offending agent (relative contraindication) and steroids

# **Drug Allergy**

- **Erythema Multiforme/Stevens-Johnson Syndrome**
  - **EM: Erythematous, polymorphic eruption caused by drugs in 10-20% cases**
    - **Includes target lesions, maculopapular rash, urticaria, vesicles – typically symmetric and on extremities**
    - **Stop offending agent immediately! Avoid in future**

# **Drug Allergy**

- **Stevens-Johnson Syndrome (EM Major)**
- **Severe form of EM with mucosal and conjunctival involvement**
- **Epidermal loss  $<10\%$  of BSA**
- **50% of cases associated with drugs (NSAIDs, sulfonamides, anticonvulsants, Allopurinol [generic])**
- **Visceral involvement associated with poor prognosis**

# **Drug Allergy**

- **Stevens-Johnson Syndrome - continued**
- **Stop offending agent immediately!  
Avoid in future**
- **Steroids (1mg/kg/day) may prevent visceral involvement and decrease duration and severity of clinical findings**

# **Drug Allergy**

- **Erythema Multiforme Lesions**
- **Three zones:**
  - **Erythematous central papule that may blister**
  - **Edematous middle ring**
  - **Erythematous outer ring**
- **Predilection for extremities**
- **Symmetrical**

# Drug Allergy

- **Toxic Epidermal Necrolysis (TEN):**
- **Acute illness characterized by fever, epidermal loss >30% of BSA**
- **Visceral involvement with high mortality (30-40%)**
- **May be difficult to distinguish from SJS (?spectrum of disease) with many of the same drugs causing both**

# Drug Allergy

- **Toxic Epidermal Necrolysis - continued**
- *Re-administration of drug likely to cause TEN and therefore is an ABSOLUTE CONTRAINDICATION!*
  - **Steroids not helpful/?contraindicated in TEN**



# **Drug Allergy**

- **Morbilliform/maculopapular exanthem**
  - **Most common drug induced skin reaction**
  - **Usually symmetric, confluent macules or papules that spare the palms/soles**
  - **Predilection for dependent areas in hospitalized patients**

# **Drug Allergy**

- **Morbilliform/maculopapular exanthem**
  - **Common drugs: PCN, NSAIDs,  $\beta$ -lactams, sulfa, anticonvulsants, Allopurinol [generic]**
  - **Removal/future avoidance of offending agent recommended. Can consider continuation if no evidence of other findings (EM/SJS, serum sickness, hypersensitivity vasculitis)**

# Drug Allergy

- **Allergy to Specific Drugs:**
- **Detecting drug-specific IgE can help assess risk for future reactions**
- **Testing includes skin testing, RAST**
- **Skin testing/RAST not helpful or indicated for non-IgE-mediated types of reactions (EM/SJS, etc)**
- **Desensitization indicated when no available substitute for offending drug**

# **Drug Allergy - Penicillin**

- **Most common cause of allergic drug reactions**
- **400-800 fatalities per year in U.S**
- **Skin test reactivity decreases by 10% annually**
- **95% of PCN metabolized to major determinant (penicilloyl)**
- **Minor determinants = remaining 5%**
  - **Allergy to minor determinants associated with severe anaphylaxis**

# Drug Allergy - Penicillin

- Skin testing available for penicillin
- Negative skin tests valid for up to 72 hrs (due to possible re-sensitization)



# **Drug Allergy - Penicillin**

- **Desensitization**
  - **For history of IgE mediated rxns only**
  - **Used only if no alternative agent**
  - **Generally performed in ICU**
- **Skin test negative/desensitized patients still considered penicillin allergic in the future**
  - **Second set negative skin tests probably predictive of no future PCN allergy**

# **Drug Allergy - Penicillin**

- **Cephalosporin and Penicillin allergy**
- **Cross reactivity is overestimated**
- **About 10% cross reactivity with first generation cephalosporin, and only 1-3% with third generation cephalosporin**
- **No standardized tests for cephalosporin as there is with PCN**
- **If PCN skin test positive: avoid or desensitize for cephalosporin**

# **Drug Allergy - Sulfa**

- **Usually manifest as maculopapular rash**
- **Rarer: urticaria/anaphylaxis/EM/SJS/TEN**
- **TMP-SMX structurally similar to sulfa-groups in HCTZ, Lasix®, and sulfonylureas: cross-sensitization is rare**
- **No reliable skin test/*in vitro* test available**
- **Desensitization by oral/IV**
- **Usually done for “no alternative therapy” (HIV+ patients needing PCP prophylaxis)**



# **Drug Allergy – NSAIDS/ASA**

- **Respiratory Triad: Nasal polyps, asthma, ASA-sensitivity**
- **Asthma often severe and steroid resistant**
- **Associated w/ chronic sinusitis**
- **Desensitization results in improvement in asthma, sinus surgeries, reduced steroids**
- **Not IgE-mediated**
- **COX inhibition: shunting arachidonic acid down leukotriene pathway**

# **Drug Allergy – NSAIDS/ASA**

- **Anaphylaxis**
  - **Usually unable to demonstrate presence of IgE**
  - **Typically do not have underlying nasal polyps, asthma, or urticaria**
  - **NSAID-anaphylaxis is typically specific to the single drug in question (not all NSAIDs), with previous sensitization required**

# **Drug Allergy**

- **Radiocontrast media (RCM)**
- **10 million studies annually in US**
- **Adverse reaction rate 5-8%**
  - **Most reactions minor**
  - **Moderate reactions in 1.0%**
  - **Life-threatening reactions 0.1%**
    - **10,000 patients annually**
  - **Mortality rate 1/75,000,130 patients/yr**
  - **Lower rates with low osmolarity RCM**

# **Drug Allergy - RCM**

- **Increased risk of reaction with:**
- **History of anaphylactoid reaction to RCM**
  - **16-44% rate of recurrent reactions**
- **Atopic/asthmatics**
- **$\beta$ -blockers/ACE inhibitors**
- **Cardiovascular disease**
- **Advanced age**
- **Female sex**
- **Receipt of large volumes of RCM**

# **Drug Allergy - RCM**

- **RCM does not contain iodine**
- **No increase risk with:**
  - **Reactions to topical iodine cleansers**
  - **Reactions to iodides**
  - **Immediate hypersensitivity to shellfish**
    - **Shellfish do not contain iodine**
    - **Shellfish allergy due to tropomyosin**
  - **Vasomotor symptoms**

# **Drug Allergy - RCM**

- **Anaphylactoid – not IgE mediated**
  - **Direct mast cell release**
- **Onset within 1-3 min, IV administration**
- **Most common:**
  - **Nausea, emesis, flushing**
- **Immediate generalized:**
  - **Urticaria-most common**
  - **Pruritus, angioedema, bronchospasm, hypotension, syncope, dysrhythmias**

# **Drug Allergy - RCM**

- **No *in vitro/in vivo* tests are available**
- **Skin testing is NOT helpful**
- **Test doses NOT helpful**
  - **Severe/ fatal reactions have occurred after 1-2 ml IV test dose**
  - **Severe reactions have followed negative test doses**

# **Drug Allergy - RCM**

- **Pre-treatment in patients with history of reaction**
  - **Corticosteroids - Prednisone [generic] 50mg PO at 13, 7 and 1 hrs before RCM administration (peds: 0.5-1 mg/kg max 50mg)**
  - **Antihistamines - Benadryl® 50mg PO/IV 1 hr before RCM administration (peds: 1 mg/kg max 50 mg)**



# **Drug Allergy - RCM**

- **If emergency study needed:**
- **Document need for study, alternatives unsatisfactory, informed consent**
- **Recommend nonionic, low osmolar RCM**

# Drug Allergy - RCM

- **Pre-treat: prednisone, benadryl, albuterol**
  - **HC 200mg IV Q4 hrs until study done AND Benadryl® 50mg IM 1 hr before RCM**
- **Proceed: emergency equipment available`**



# **Drug Allergy**

- **Local anesthetics**
- **Immediate type reactions described, rarely proven**
- **Allergic mechanism often blamed for:**
- **Pharmacologic action**
  - **CNS effects (excitatory, depressant)**
  - **CV effects (Bradycardia, Afib, Hypotension, cardiovascular collapse)**

# **Drug Allergy**

- **Local anesthetic reactions – causes**
  - **Epinephrine side effect**
  - **Vasovagal syncope**
  - **Hyperventilation**
  - **Anxiety reaction**
  - **Preservatives - may be IgE mediated**
    - **sodium bisulfites in spinal anesthesia**
    - **methylparabens in multi-dose vials**
  - **Latex containing products**

# **Drug Allergy**

- **Local anesthetics – management**
- **Refer to allergist for testing**
  - **Provocative, graded dose testing**
  - **Goal is to tolerate 3 ml of the chosen agent**
- **Skin testing should be completed shortly before the anticipated procedure**

# Stinging Insect Allergy

- **Earliest report of stinging insect reaction**
- **Hieroglyphics on the wall of King Menses' Egyptian tomb**
- **He apparently died of a wasp or hornet sting in 2661 B.C.**



# **Stinging Insect Allergy**

- **Local reactions: 85%**
- **Large local reactions: 10 - 15%**
- **Systemic reactions: 0.5 - 5%**
  - **0.4 - 0.8% of children; 3% of adults**
- **40 - 150 deaths / year in U.S.**
  - **5% of fatalities < age 20**
  - **80% of fatalities > age 40**
  - **40% of fatalities had NO history of prior sting reaction**

# **Stinging Insect Allergy**

- **9 -32% of general population have venom-specific IgE on RAST**
  - **Presence of IgE venom antibody not necessarily predictive of clinical sensitivity**
  - **Skin testing not indicated for asymptomatic persons**



# Stinging Insect Allergy

- **The Culprits:**
  - **Yellow Jacket**
  - **Hornet**
  - **Wasp**
  - **Honeybee**
  - **Fire Ant**



# Stinging Insect Allergy

- **Yellow Jacket**
  - Aggressive, easily provoked
  - Often around food, trash
  - Higher risk of infection, cellulitis
  - Retractable stinger



# Stinging Insect Allergy

- The Hornet
- Large, differing colors
- Large papier-maché nests in trees & buildings
- Active at night, seek light



# Stinging Insect Allergy

- **Wasp**
- **Long legs, slender waist**
- **Paper-comb nests**
  - made from plant fibers
  - found under eaves & rafters
- **15-200 individuals per nest**
- **Not aggressive unless threatened**
- **Stinger retractable - can sting many times**



# Stinging Insect Allergy

- **Honeybee**
  - **Attacks only when threatened**
  - **Barbed stinger, eviscerates insect**
- **Stout, hairy body**
- **Attracted to bright colors**
- **Found around lawns, flowering plants**
- **Large colonies >65,000**
- **Cross reacts with bumblebee**



# Stinging Insect Allergy

## ■ Fire Ant

- Live in above-ground mounds, large colonies
- Rapid, Aggressive, when mound is disturbed or after a food source
- Bite repeatedly
- Sting – localized, intense burning and pustules



# **Stinging Insect Allergy**

- **Reactions: Local**
  - **Most stings cause local reactions**
  - **Pain, swelling, erythema at site of sting**
  - **May be accompanied by itching**
  - **Last from hours to a few days**
  - **No specific treatment required**
  - **Ice, antihistamine, analgesics help**

# **Stinging Insect Allergy**

- **Large local reactions**
  - **Occur in 10-15% of adults**
  - **Swelling >10cm or crossing a joint**
  - **Peaks at 24-48 hrs, lasts 5-7 days**
  - **Subsequent stings usually also large local RXN (90-95%)**
  - **Does NOT tend to progress to anaphylaxis (5-10%)**
- **Skin testing and ITx NOT indicated**



# **Stinging Insect Allergy**

- **Anaphylaxis**
  - **Usually occurs within 20 min; reports up to 72 hrs**
  - **Same symptoms as other anaphylaxis**
  - **50-60 % chance of recurrence with subsequent stings**
  - **Skin testing and immunotherapy indicated**

# **Stinging Insect Allergy**

- **Toxic**
  - **Due to multiple stings**
  - **Myalgias**
  - **Fever / chills**
- **Serum sickness (7-14 days following sting)**
- **Neuritis, glomerulonephritis, encephalitis**
- **Vasculitis (1-2 days following sting)**
- **Guillan Barré**

# **Stinging Insect Allergy**

- **Imported Fire Ant**
- **Imported from South America at Mobile, Alabama (soil in ballast) in 1918 – 1930s**
- **0.6-6% incidence of anaphylaxis**
- **Local reaction forms sterile pustule**
- **Keep clean to avoid infection, cellulitis**
- **Treat anaphylaxis as usual**
- **Immunotherapy available**

# **Stinging Insect Allergy**

- **Management: Avoidance**
  - **Kill or relocate the offending insects**
  - **Don't dress or smell like a flower**
  - **Cover exposed skin**
    - **wear shoes/socks/long pants/long sleeved shirt/gloves**
- **Self injectable epinephrine**
- **Refer for evaluation for Immunotherapy (IT) → systemic reaction risk ↓ to 2-3%**

# **Stinging Insect Allergy**

- **Treatment Summary**
  - **Anaphylaxis: Immunotherapy, Epipen**

# **Stinging Insect Allergy**

- **Special case:**
  - **Cutaneous reaction only (urticaria, angioedema) in person <16 years old**
    - **Immunotherapy not indicated**
    - **Risk of worse reaction only 5 - 10%**
- **Local / Large local:**  
**no immunotherapy**

# **Stinging Insect Allergy**

- **Immunotherapy for Hymenoptera**
- **Buildup - Gradual increasing doses of venom, SQ**
  - **Takes several months; can “rush”**
- **Maintenance - typically q4 week interval**
- **Duration - 5 years, lifelong if initial reaction life-threatening**
  - **Indefinitely if reaction to field sting or systemic reaction on ITX**

# **Urticaria and Angioedema**

- **Overview**
- **Definitions / epidemiology**
- **Pathogenesis**
- **Differential diagnosis**
- **Evaluation**
- **Treatment**
- **Natural history**



# **Urticaria - Definition**

- **Pruritic, erythematous elevations that blanch with pressure**
- **Wax and wane over time**
- **Capillary dilatation in superficial dermis**
- **Dermal edema**
- **Mild perivascular infiltrate of lymphocytes, eosinophils and neutrophils.**
- **Common name: Hives**

# **Angioedema - Definition**

- **Well-demarcated swelling of deep skin structures**
- **Predilection for face, tongue, extremities, and genitalia**
- **May be painful or burning**
- **Little or no pruritus**
- **Nonerythematous**
- **Asymmetric distribution**

# **Urticaria/Angioedema - Definitions**

## **Acute urticaria/angioedema**

- **< 6 weeks in duration**
- **Children and young adults**
- **Increased incidence in atopics**
- **Most common identifiable cause is viral infection >> meds, idiopathic, foods**

# **Urticaria/Angioedema - Definitions**

## **Chronic urticaria/angioedema**

- **>6 weeks in duration**
- **80-90% idiopathic**
- **Up to 20% physical urticaria**
- **M:F = 1:2 (middle-aged females)**
- **<2% related to food allergens in adults**
- ***Rarely* IgE mediated**

# **Urticaria/Angioedema - epidemiology**

## **Chronic Urticaria/Angioedema: Presentation -**

- **50% urticaria and angioedema**
- **40% urticaria alone**
- **10% angioedema alone**



# **Urticaria/Angioedema - Pathophysiology**

## **Mast cell degranulation**

- **Immunologic mechanisms**
  - **IgE mediated allergy**
  - **Autoimmune phenomena**
  - **Complement disorders**
- **Physical causes**
- **Direct membrane activators**
- **Associated with neoplasm and infections**

# **Urticaria/Angioedema**

- **Differential Diagnosis**
- **Non-urticarial diseases**
  - **Bullous pemphigoid**
    - **Early lesions pruritic and urticarial**
    - **Limited disease may not blister**
    - **Characteristic skin biopsy**

# **Urticaria/Angioedema – Differential Diagnosis**

- **Dermatitis herpetiformis**
  - **Early lesions urticarial**
  - **Associated with gluten-sensitive enteropathy**
  - **Distributed on buttocks/ extensor surfaces**



# **Urticaria/Angioedema – Differential Diagnosis**

- **Erythema multiforme**
  - **Individual lesions last >24hr**
  - **Painful/tender**
  - **Acrally distributed**
  - **Target lesions**

# **Urticaria/Angioedema – Differential Diagnosis**

- **Pruritic Urticarial Papules and Plaques of Pregnancy (PUPPP)**
- **Urticaria in and around abdominal striae**
- **Lesions may spread to extremities**
- **Face, palms and soles usually spared**

# **Urticaria/Angioedema – Differential Diagnosis**

- **Usually begins in 3<sup>rd</sup> trimester, may occur postpartum**
- **Often resolves a few weeks after delivery**

# **Urticaria/Angioedema – Specific Causes: Physical**

- **Cold urticaria**
- **Comprises 2% of all urticaria**
- **Onset within minutes of warming**
- **Cold food may cause oral swelling or GI upset**
- **Lacrimation, salivation, diarrhea, anaphylaxis**
- **Diagnose with ice cube test**

# **Urticaria/Angioedema – Specific Causes: Physical**

- **Cholinergic urticaria (heat induced)**
  - **Punctate wheals with large flare**
  - **Increased body temp, exercise, hot shower and strong emotions**
  - **4% of urticaria**

# Urticaria

- Pressure
  - **Dermatographism**
  - **Delayed**
  - **3-6 hours after pressure**
  - **Palms, soles, buttocks**

# Urticaria

- **Solar**
  - **Sensitivity to specific wavelengths**
  - **Six types**
  - **Type VI associated with porphyria**



# **Urticaria**

- **Urticaria pigmentosa (UP)**
  - **Common cutaneous manifestation of systemic mastocytosis**
  - **Hyper-pigmented papules**
  - **Darier's sign: linear hive when lesions stroked**
  - **50% of Peds UP resolves by adulthood**



# Angioedema

- **ACE-inhibitor induced**
- **Decrease in bradykinin metabolism**
- **0.1-0.2% of patients on ACE-inhibitors**
- **Onset within hours to weeks**
  - **May occur years into therapy**
- **Facial / glossal edema most often**
- **Treatment is discontinuation of ACE-inhibitor**

# Urticaria/Angioedema

- Neoplasms
- GI
- Lung
- Lymphoid

# **Urticaria/Angioedema**

- **Infectious**
- **Viral**
  - **HSV, HAV, HBV, HCV, EBV, Coxsackievirus**
- **Bacterial**
  - **Streptococcus, Spirochete, H. pylori**
- **Helminthic parasites**
- **Mycoplasma**

# **Urticaria/Angioedema - Evaluation**

- **History**
- **Physical**
  - **Dermatophytes**
  - **Lymphadenopathy**
  - **Organomegaly**
  - **Abdominal masses**
  - **Urticaria pigmentosa**

# **Urticaria/Angioedema - Evaluation**

- **Screening labs**
- **CBC with differential**
- **ESR**
- **UA**
- **LFT's**

# Urticaria/Angioedema- other labs

- Stool for O&P
- RPR
- EBV
- ANA
- Cryoglobulins
- Hepatitis panel
- C4, CH<sub>50</sub>
- C1 Inhibitor
- TSH and anti-thyroid antibodies
- Food skin tests and elimination diet

# **Urticaria/Angioedema- biopsy criteria**

- **Single lesions > 24 hours**
- **Purpuric component**
  - **Residual pigmentation**
  - **Lower extremity prominence**
- **Non-pruritic**
- **Constitutional symptoms**
- **Cluster around joints**
- **Refractory to therapy**

# **Urticaria/Angioedema- Treatment**

- **Removal of stimulus**
- **Avoidance of precipitators**
- **Antihistamine prophylaxis**
- **For severe or life threatening symptoms**
  - **Epinephrine 0.3cc 1:1000 IM**
  - **Steroids**
  - **Medic Alert bracelet**



# **Urticaria/Angioedema - Prognosis**

- **1/2 resolve within 6 months**
- **2/3 resolve within 3 years**
- **4/5 resolve within 10 years**
- **1-2% persist for 20-25 years**

# **Urticaria/Angioedema - Summary**

- **Urticaria is a symptom not a disease**
- **Work up is based on detailed Hx & Px**
- **Avoid unnecessary lab tests**
- **Primary Rx: continuous antihistamines**
- **Allergy consult if**
  - **Acute: life threatening event**
  - **Chronic: > 6 weeks duration**

# **Hereditary Angioedema**

- **Recurrent attacks**
- **No urticaria or pruritus**
- **May be precipitated by trauma**
- **Duration of hours to days**
- **Facial, glossal, laryngeal (potentially life-threatening), or GI involvement**

# **Hereditary Angioedema**

- **Autosomal dominant**
- **85% reduced Clq esterase inhibitor (C1 inh)**
- **15% abnormal C1 inh function**
- **Baseline low C4 (best screen)**
- **Decreased C2 during attacks**

# **Hereditary Angioedema**

## **Treatment for acute events**

- **Epinephrine 0.3 cc 1: 1000**
- **Airway**
- **2 units FFP before surgeries**
- **Purified C1 esterase inhibitor**
  - **Very expensive**
  - **Available in U.S. on case by case basis**

# **Hereditary Angioedema**

## **Long-term management of recurrent attacks**

- **Androgen derivatives**
  - **Danazol or Stanozolol [generics]**
- **Aspirin**

# References

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